

## REMARKS

Claims 1-25 were pending in this application. Claims 6, 7, 12, 14, 15, and 19-23 are now cancelled without prejudice to Applicants' right to prosecute their subject matter in the present application and in related applications. Claims 8-9 stand presently withdrawn from consideration as being directed to non-elected species. Applicants understand that claims 8-9 will be examined upon allowance of generic claims. New claims 26-29 are added and claims 1, 3-5, 11, 13, 16, 17, and 24 are currently amended without any intent of disclaiming equivalents thereof. Accordingly, claims 1-5, 10, 11, 13, 16-18, and 24-29 are pending and presented for consideration.

### Specification amendments

Applicants have amended the specification to introduce sequence identifiers and to correct typographical errors. Applicants respectfully submit the amendments to the specification introduce no new matter.

### Claim amendments

Support for the claim amendments can be found in the specification, including the claims as originally filed. Support for the recitation of "Fc<sub>m</sub>-L-EPO<sub>m</sub>" in amended claim 1 is found in the specification at least, for example, at page 10, line 31 to page 11, line 5. Support for the recitation of "and comprises at least one of the following changes: Asn<sub>24,38,83</sub> -> Gln, Ser<sub>126</sub> -> Ala, His<sub>32</sub> -> Gly, Ser<sub>34</sub> -> Arg, and Pro<sub>90</sub> -> Ala" in amended claim 1 is found in the specification at least, for example, at page 10, lines 1-6, and in original claim 6. Support for the recitation of "and which ends C-terminally at the amino acid positions 108, 98, 93, 88, 85 or 77 of EPO" in amended claim 1 is found in the specification at least, for example, at page 8, lines 7-8, and in original claim 7. Claim 1 has also been amended to delete unnecessary words. Support for the recitation of "comprising" in amended claim 16 is found in the specification at least, for example, at page 16, lines 19-20. Claims 3-5, 11, and 24 have been amended for consistency with independent claim 1 from which they depend. Claim 13 has been amended to remove a

reference to a non-elected invention. Claims 1, 3, 17, and 24 have also been amended to correct typographical errors and for clarification.

Support for new claim 26 is found in the specification at least, for example, at page 10, line 31 to page 11, line 5; at page 12, lines 31-34; and in original claims 1 and 12. Support for new claim 27 is found in the specification at least, for example, at page 13, lines 1-3, and in original claim 14. Support for new claim 28 is found in the specification at least, for example, at page 13, lines 17-21. Support for new claim 29 is found in the specification at least, for example, at page 15, lines 5-13.

Applicants submit that these amendments introduce no new matter.

#### Sequence listing

Applicants have amended the Sequence Listing to include sequences disclosed in the specification at page 30, line 4, and page 37, line 15. Applicants submit that the amendments introduce no new matter. Please replace the prior Sequence Listing with the enclosed pages marked "Sequence Listing."

#### Telephonic interview

Applicants thank Examiner DeBerry and Examiner Kemmerer for the telephonic interview on July 24, 2003, in which it was determined that claims to non-elected species need not be cancelled at this time.

The following comments address in order the remaining issues raised in the Office action.

#### Sequence Rules

The Office action required insertion of a sequence identifier at page 37, line 15. Applicants have amended the application accordingly and submit that the application fully complies with 37 C.F.R. §§ 1.821-1.825.

Claim Objections

The Office action objects to claims 1, 6, 10, 12, 13, 14, 17, and 18 for encompassing non-elected inventions and/or species. Without acquiescing to the objection, and solely to advance prosecution, Applicants have cancelled claims 6, 12, and 14; the objection with respect to claims 6, 12, and 14 is therefore moot. Applicants traverse the objections to claims 1, 10, 17, and 18, and request that the objections be held abeyance until allowable subject matter is determined. Applicants have amended claim 13 to remove reference to a non-elected invention. Applicants respectfully request reconsideration and withdrawal of the objection with respect to claim 13.

Claim Rejections Under 35 U.S.C. § 112, second paragraph

Claims 1, 5 and 16 stand rejected under 35 U.S.C. § 112, second paragraph. The Office action alleged that claim 1 was rendered indefinite by its recitation of "an erythropoietin (EPO) form having improved properties." As amended, claim 1 no longer recites "having improved properties." The Office action alleged that claim 5 was rendered indefinite by depending from non-elected species of claim 1. Applicants traverse this rejection. As acknowledged by Examiners DeBerry and Kemmerer during the telephonic interview, there is no need to cancel non-elected species at this stage. The Office action further alleged that claim 16 was rendered indefinite by its recitation of "a fusion protein according to claim 1, said fusion protein being a whole Ig molecule." Applicants have amended claim 16 to recite "a fusion protein according to claim 1, said fusion protein comprising a whole Ig molecule." In view of the amendments and the remarks, Applicants respectfully request reconsideration and withdrawal of the rejection.

Claim Rejections Under 35 U.S.C. § 102

Claims 1-6, 16-18, 24, and 25 stand rejected under 35 U.S.C. § 102(a) as allegedly anticipated by WO 99/02709 ("Sytkowski"). Claim 6 has been cancelled. Applicants traverse the rejection of claims 1-5, 16-18, 24, and 25.

As amended, claim 1 relates to fusion proteins comprising (i) EPO<sub>m</sub> or (ii) partially sialylated EPO or (iii) truncated EPO and/or (iv) a linker which has no protease cleavage site. Applicants note that Fc-EPO<sub>m</sub> is currently under examination. EPO<sub>m</sub> in claim 1 is "EPO which is mutated but not truncated in its amino acid sequence and comprises at least one of the following changes: Asn<sub>24,38,83</sub> -> Gln, Ser<sub>126</sub> -> Ala, His<sub>32</sub> -> Gly, Ser<sub>34</sub> -> Arg, and Pro<sub>90</sub> -> Ala." Sytkowski does not teach or suggest a fusion protein comprising an EPO comprising an amino acid change at position 24, 32, 34, 38, 83, 90, or 126, as set forth in amended claim 1. Accordingly, Applicants submit that Sytkowski does not anticipate claim 1 or any claim (*e.g.*, 2-5, 16-18, 24, and 25) depending from claim 1.

Applicants respectfully request reconsideration and withdrawal of the rejection.

#### Claim Rejections Under 35 U.S.C. § 103

Claims 10-13 and 14 stand rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Sytkowski in view of U.S. Patent No. 5,888,772 ("Okasinski"). Applicants have cancelled claims 12 and 14 without prejudice. Applicants respectfully traverse the rejection of claims 10, 11, and 13.

The appropriate criteria for the determination of obviousness under 35 U.S.C. § 103 is whether the prior art would have suggested to one of ordinary skill in the art that the claimed subject matter should be carried out and would have a reasonable likelihood of success. Both the suggestion and the expectation of success must be founded in the prior art, not in Applicant's disclosure. *In re Dow Chemical Company*, 837 F.2d 469,473, 5 U.S.P.Q.2d 1529, 1531 (Fed. Cir. 1988). That is, obviousness cannot be established by combining the teachings of the prior art to produce claimed invention, absent some teaching or suggestion or incentive in the art supporting the combination. *In re Fine*, 5 U.S.P.Q.2d 1596 (Fed. Cir. 1988). Cited references which merely indicate the isolated elements recited in the claims is not a sufficient basis for concluding that the combination would have been obvious. *Ex parte Hiyamaizu*, 10 U.S.P.Q.2d 1393 (BPAI 1988).

For the reasons set forth below, Applicants respectfully submit that neither Sytkowski nor Okasinski suggests their combination, and that neither Sytkowski nor Okasinski provides a reasonable expectation of success, were such a combination to be made.

As amended, claim 1 relates to fusion proteins comprising (i) EPO<sub>m</sub> or (ii) partially sialylated EPO or (iii) truncated EPO and/or (iv) a linker which has no protease cleavage site. Applicants note that Fc-EPO<sub>m</sub> is currently under examination. EPO<sub>m</sub> in claim 1 is "EPO which is mutated but not truncated in its amino acid sequence and comprises at least one of the following changes: Asn<sub>24,38,83</sub> -> Gln, Ser<sub>126</sub> -> Ala, His<sub>32</sub> -> Gly, Ser<sub>34</sub> -> Arg, and Pro<sub>90</sub> -> Ala." Claims 10, 11, and 13 depend from and, therefore, incorporate all the limitations of independent claim 1.

Sytkowski teaches fusion proteins allegedly having increased EPO biological activity. *See, e.g.*, page 2, lines 11-21. However, Sytkowski does not teach or suggest a fusion protein comprising an EPO comprising an amino acid change at position 24, 32, 34, 38, 83, 90, or 126, as set forth in amended claim 1. Applicants further submit that Sytkowski cannot be combined with Okasinski to produce an EPO fusion protein that would render obvious the invention of claim 1.

Okasinski does not teach or suggest preparing a fusion protein with an amino acid change at position 24, 32, 34, 38, 83, 90, or 126. Okasinski does not teach or suggest an amino acid change at position 32, 34, or 90 of EPO. Furthermore, Okasinski teaches that amino acid substitution at position 24, 38, 83, or 126 severely reduces the biological activity of EPO. *See, e.g.*, column 3, lines 15-27. Therefore, Applicants submit that Okasinski provides no motivation to introduce an amino acid modification at position 24, 32, 34, 38, 83, 90, or 126 into Sytkowski's EPO fusion protein, in which increased biological activity is sought.

Indeed, Okasinski teaches away from the invention of claim 1. "A reference may be said to teach away when a person of ordinary skill, upon reading the reference, would be . . . led in a direction divergent from the path that was taken by the applicant . . . ." Tec Air, Inc. v. Denso Mfg. Mich. Inc., 192 F.3d 1353, 1360 (Fed. Cir. 1999). As set forth at column 3, lines 15-27, Okasinski teaches that a series of EPO mutant proteins with a single amino acid substitution at

position 24, 38, 83, or 126 show *severely reduced biological activity*. Therefore, Applicants submit that a person of ordinary skill, upon reading Okasinski, would be discouraged from introducing an amino acid change at position 24, 38, 83, or 126 into an EPO fusion protein of Sytkowski. As discussed above, Sytkowski seeks an EPO fusion protein with increased biological activity, while Okasinski teaches that an amino acid modification at position 24, 38, 83, or 126 severely reduces the biological activity of EPO. If a reference teaches away from the claimed invention, the reference cannot support a rejection under 35 U.S.C. § 103. See MPEP § 2145(X)(D); see also Winner Int'l Royalty Corp. v. Wang, 202 F.3d 1340 (Fed. Cir. 2000) (affirming district court finding that a U.S. patent, in disclosing disadvantages of exposed locking mechanisms, taught away from their use). Furthermore, Applicants submit that the cited references provide no reasonable expectation of success even if the teachings of Okasinski were to be combined with those of Sytkowski.

Accordingly, Applicants submit Sytkowski and Okasinski do not render obvious claim 1 or any claim depending directly or indirectly from claim 1 (*e.g.*, claim 10, 11, or 13). Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection.

New claims 26-29 relate to a fusion protein that comprises EPO comprising Cys at position 88. Neither Sytkowski nor Okasinski teaches or suggests a protein comprising EPO with Cys at position 88. Accordingly, Applicants submit that even in combination Sytkowski and Okasinski cannot render obvious the invention of claims 26-29.

### CONCLUSION

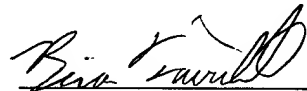
Claims 1-5, 10, 11, 13, 16-18, and 24-29 are pending and presented for consideration.  
The Examiner is invited to telephone the undersigned agent to discuss any remaining issues.

Respectfully submitted,

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